REMARKS

Applicant acknowledges with gratitude the withdrawal by the PTO of the finality of the previous office action. Claim 16 is pending in the present application and stands rejected further to the non-final Office Action mailed by the PTO on February 2, 2007. New claim 17 has been added to more particularly point out and distinctly claim subject matter which the Applicant regards as encompassed by the claimed embodiments. Support for claim 17 may be found in the specification, for example, at page 6, lines 10-14, at page 7, lines 3-4, at page 10, lines 2-4, and at page 14, lines 6-8 and line 25 through page 16, line 22. No new matter has been added by way of the present amendment.

REJECTION UNDER 35 U.S.C. §103

Claim 16 stands rejected under 35 U.S.C. §103 for alleged obviousness over Cole (1999 *BioTechniques* 26:748) in view of Coen et al. ("The Polymerase Chain Reaction," in Ausubel et al., (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, Inc., Chapter 15, Sections 1-8, 2003). More specifically, the PTO asserts that Cole teaches gellan electrophoresis gels having gellan concentrations as low as 0.03% and more typically 0.1%. The PTO concedes that Cole does not disclose gellan gels that comprise a DNA polymerase, dNTPs and a target nucleic acid. The PTO then alleges that Coen et al. teach mixing, *inter alia*, DNA polymerase, dNTPs and a target nucleic acid in a first step of PCR, and subsequently displaying PCR products on an appropriate gel. The PTO alleges further that at the time the present application was filed, a person having ordinary skill in the art would have been motivated by Cole to apply the advantages of the gellan gel described therein to display PCR reaction products produced according to Coen et al.

Applicant respectfully traverses the rejection. The presently claimed embodiments are directed to a composition suitable for use in nucleic acid amplification comprising water, gellan at a concentration above 0.005 wt% based on the weight of water, a DNA polymerase, dNTPs, and a target nucleic acid.

For reasons discussed herein, the PTO fails to establish a *prima facie* case of obviousness where the disclosure of the present application would not have been predicted by a

person having ordinary skill in the art, and where the prior art, if anything, teaches away from the claimed combination.

The person having ordinary skill in the art would not have predicted that PCR can proceed in the presence of gellan. The presently claimed embodiments derive from the surprising discovery that the polymerase chain reaction (PCR) for nucleic acid amplification can proceed in the presence of gellan, as clearly disclosed in the present specification, for instance, at page 5, line 25 through page 6, line 6; *see also* page 14, lines 3-24. In particular, and as disclosed therein, the presently claimed subject matter is unexpected, in part because gellan sequesters Mg^{2+} in the course of gel formation (*e.g.*, specification at page 14, lines 13-24). Based on the sequestration of Mg^{2+} by gellan, the ordinarily skilled person would reasonably have expected that in the presence of gellan the Mg^{2+} would be unavailable to participate in the PCR mechanism, where it is well known in the art that PCR reactions absolutely depend upon Mg^{2+} for activity.

Accordingly, the person having ordinary skill in the art would not have expected PCR to proceed if a nucleic acid amplification reaction mixture comprised gellan, and so would not have contemplated gellan according to the presently recited composition *for use in nucleic acid amplification*. Remarkably, however, the present application discloses for the first time that PCR does in fact proceed in the presence of gellan, as shown in the Examples at pages 17-25. Furthermore, and wholly unexpectedly, the sensitivity of PCR conducted in the presence of gellan was enhanced (*e.g.*, page 7, lines 1-4) relative to that seen for PCR reactions performed in the absence of gellan (*e.g.*, page 23, line 1 through page 25, line 2).

The person having ordinary skill in the art would not have been motivated by the prior art to arrive at the claimed composition. Applicant traverses the assertion made by the PTO at page 3 of the Action that "[o]ne of ordinary skill in the art would have been motivated to do this [use the Cole gellan electrophoresis gel for displaying the PCR products of a PCR reaction] since gellan gum serves as an alternative gel material which allows for easy recovery of DNA . . .". Applicant submits that this assertion is beside the point. Specifically, the PTO has failed to provide any evidence or reasoning why the person having ordinary skill in the art would have been motivated to use the Cole gellan electrophoresis gel for displaying PCR products, and much

less for use *in* nucleic acid amplification, *i.e.*, for purposes of conducting such amplification in the presence of gellan.

The PTO concedes that the teachings of the prior art are limited to a step of *amplifying* nucleic acid (*e.g.*, preparing a PCR reaction mixture) that is temporally separated from the step of subsequently *displaying* amplification products (*e.g.*, separating DNA on an electrophoretic gel), where for reasons given herein, prior to the present application the art failed to provide the use of gellan gels for nucleic acid amplifications such as PCR. The documents cited by the PTO fail in any way to contemplate a composition in which the discrete event of nucleic acid amplification takes place with gellan present. By way of contrast, the presently claimed subject matter provides a composition suitable for nucleic acid amplification that comprises, *e.g.*, a PCR reaction mixture *and* gellan, which composition is nowhere even remotely suggested by the art, and which composition would not have been expected to support successful amplification, for reasons discussed herein.

Cole teaches *away* from the claimed invention by disclosing that gellan is not an appropriate electrophoretic medium if it interferes with the intended use of DNA. Contrary to the assertions made by the PTO, Applicant submits that the combination of gellan and divalent cation-dependent nucleic acid amplification reactions would have been regarded as incompatible to the ordinarily skilled person. Cole notes, for example, that ideal criteria for a reversible gel include "that the presence of the gel-forming material not interfere with the applications the DNA will be used for" (at page 749, left-hand column, twelve lines from bottom to nine lines from bottom). Therefore, in view of Cole the person of ordinary skill in the art would not reasonably have expected successfully to practice the subject matter encompassed by the present claims, because the Mg^{2+}-dependent PCR reaction would not be able to proceed due to entrapment of the divalent cation by gellan.

Cole teaches *away* from the claimed invention by disclosing that divalent cations, which as noted above are essential for PCR, in fact weaken gellan gels. Cole teaches that the use of divalent cations in gellan gels can hinder gel preparation (*e.g.*, page 750, left-hand column, last paragraph) and that inclusion of Mg^{2+} in particular results in weakened gellan gels (*e.g.*, page 754, left-hand column, ten lines from bottom to seven lines from bottom). The skilled person

would therefore not have been motivated, by Cole in combination with any other knowledge in the art at the time of filing, to arrive at the subject matter of the instant claims with the requisite reasonable expectation of success because these teachings of Cole would if anything discourage the use of Mg^{2+}, a prerequisite for nucleic acid amplification via PCR, in gellan compositions.

Furthermore, the person having ordinary skill in the art would not have been motivated to use, for nucleic acid amplification, even the gellan gels of Cole that do not require divalent cations for gel formation. On this point, even assuming *arguendo* that the skilled person were to infer from Cole that because in such gels divalent cations are not required for gel formation and so might be available for other purposes such as amplification reactions (which Applicant hastens to point out is an assumption founded on not one scintilla of evidence that is provided by Cole), Cole emphasizes the importance of maintaining a pH below 7.0 in such divalent cation-free gellan gels (page 752, first full paragraph starting in center column). Such a pH restriction would be incompatible, however, with common nucleic acid amplification reactions such as the PCR conditions of Coen et al., which typically feature pH values above 7.0. As such, Applicant submits that given Cole alone or in combination with Coen et al. or any other knowledge in the prior art, the person having ordinary skill in the art would have had no motivation to arrive at the presently recited composition for use in nucleic acid amplification.

Coen et al. fail to remedy the shortcomings of Cole and are silent regarding gellan. The PTO cites Coen et al. for nothing more than disclosing basic and well-known components of PCR reaction mixtures such as DNA, DNA polymerases, dNTPs, etc., and in this respect Coen et al. are merely cumulative with references cited in the present application at page 14, line 25 through page 16, line 21, and in the Examples. Coen et al. fail, however, to remedy the deficiencies of Cole, insofar as Coen et al. are absolutely silent with respect to any suggestion whatsoever to include gellan in a composition for nucleic acid amplification. Coen et al. merely teach Mg^{2+} concentrations and other reaction conditions for use in PCR. Based on Cole, the person having ordinary skill in the art would expect the Mg^{2+} concentrations of Coen et al. to weaken gellan gels and the pH restrictions of divalent cation-free gels to be unsuitable for nucleic acid amplification (for reasons also discussed above), and so would not have been motivated to practice the claimed invention with a reasonable expectation of success. As also

noted above, given the teachings of Coen et al., the skilled person would recognize that the typical pH conditions for nucleic acid amplification reactions are incompatible with divalent cation-free gellan gel formulations of Cole, and so would not have any expectation of successfully arriving at the presently claimed composition.

Moreover, neither Cole nor Coen et al. alone or in combination –nor any other knowledge in the prior art of which the PTO can provide evidence-- suggest that it might be at all desirable to combine their teachings by preparing a composition for nucleic acid amplification such as PCR in the presence of any gel material, much less specifically using gellan gel. Accordingly, Applicant submits that the PTO impermissibly employs hindsight in view of the teachings of the present application by asserting the combination of Cole and Coen et al., neither of which in any way relates to the recited composition suitable for use in nucleic acid amplification that, in pertinent part, comprises gellan.

Additionally, Applicant respectfully points out that the United States Supreme Court has recently noted that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (April 30, 2007, No. 04-1350), citing *United States v. Adams*, 383 U.S. 39. For reasons given above, Applicant submits that in the instant application, the PTO has done nothing more than assert that the art was aware of the separate and independent elements of gellan on the one hand, and PCR reaction components (DNA polymerase, dNTPs, target nucleic acid) on the other, and that such an assertion falls short of establishing *prima facie* obviousness of the encompassed subject matter. Accordingly, reconsideration of the application in view of the present Remarks, and withdrawal of the rejection under 35 U.S.C. §103, are respectfully requested.

INFORMATION DISCLOSURE STATEMENT

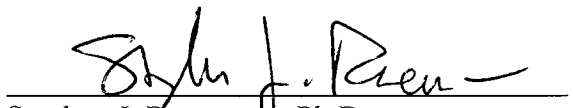
The undersigned requests that the Examiner please initial the Chetvernia et al. reference from the Information Disclosure Statement of November 1, 2004.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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